Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Abnormal uterine bleeding in pre-menopausal women.

Bibliographic Source(s)

Singh S, Best C, Dunn S, Leyland N, Wolfman WL, Clinical Practice Gynaecology Committee. Abnormal uterine bleeding in pre-menopausal women. J Obstet Gynaecol Can. 2013 May;35(5 eSuppl):S1-28. [156 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The quality of evidence assessment (I-III) and classification of recommendations (A-D, L) are defined at the end of the "Major Recommendations" field.

Introduction

Summary Statement

- Abnormal uterine bleeding (AUB) is a common condition affecting women of reproductive age that has significant social and economic impact. (II-2)

Definitions

Summary Statements

- Contemporary terminology used to describe AUB in reproductive-aged women aims to simplify definitions and to provide standard descriptions related to patient presentation. (III)
- The consequences of AUB on an individual's overall health determines the degree to which intervention may be required. (II-2)

Recommendation

1. Adoption of standardized international terminology for AUB should be considered. (III-C)

Evaluation

History, Physical Examination and Laboratory Investigations

Summary Statement

- A thorough history and physical examination will often indicate the cause of AUB and direct the need for further investigation and treatment. (III)

Recommendations

2. A complete blood count is recommended for women with heavy or prolonged bleeding. (II-2A)
3. If there is any possibility of pregnancy, a sensitive urine or serum pregnancy test should be performed. (III-C)
4. Testing for coagulation disorders should be considered only in women who have a history of heavy menstrual bleeding beginning at menarche or who have a personal or family history of abnormal bleeding. (II-2B)
5. Thyroid function tests are not indicated unless there are clinical findings suggestive of an index of suspicions of thyroid disease. (II-2D)

Imaging and Pathology

Clinical Tips
1. Ultrasound endometrial assessment: The endometrium is measured as the maximum anterior-posterior thickness of the echo on a long-axis transvaginal view of the uterus. The normal endometrium in a premenopausal woman varies in thickness according to the menstrual cycle from 4 mm in the follicular phase up to 16 mm in the luteal phase. 2. Saline infusion sonohysterography (SIS) is a useful imaging modality prior to planned hysteroscopic or laparoscopic procedures for fibroids, polyps, and uterine anomalies to ensure safe and appropriate interventions.

Summary Statement

- Imaging and hysteroscopy offer the clinician additional information to assist in patient assessment and treatment in indicated circumstances. (I)

Recommendations

6. If imaging is indicated, transvaginal ultrasound should be the first line imaging modality for AUB. (I-A)
7. SIS and diagnostic hysteroscopy should be used in the diagnosis and characterization of discrete intrauterine abnormalities such as submucosal fibroids. (I-A)

Endometrial Assessment and Biopsy

Clinical Tips
1. Indications for endometrial biopsy in women with AUB: • Age >40 • Risk factors for endometrial cancer (see Table 2.4 in the original guideline document) • Failure of medical treatment • Significant intermenstrual bleeding 2. Consider endometrial biopsy in women with infrequent menses suggestive of anovulatory cycles.

Recommendations

8. Endometrial biopsy should be considered in bleeding women over age 40 or in those with bleeding not responsive to medical therapy, as well as in younger women with risk factors from endometrial cancer. (II-2A)
9. Office endometrial biopsy should replace dilation and uterine curettage as the initial assessment of the endometrium for these women. (II-2A)
10. Focal lesions of the endometrium that require biopsy should be managed through hysteroscopy-guided evaluation. (II-2A)

Medical Treatment

Hormonal Treatments

Clinical Tip
The long-term use of gonadotropin releasing hormone (GnRH) agonists in the setting of abnormal bleeding should be limited to scenarios in which other medical or surgical treatments are contraindicated.

Summary Statements

- Once malignancy and significant pelvic pathology have been ruled out, medical treatment is an effective first line therapeutic option for AUB. (I)
- Medical treatment tailored to the individual woman's therapeutic goals, desire for contraception, underlying medical conditions, and tolerance of side effects will encourage compliance and maximize the likelihood of treatment success. (III)

Recommendations

11. Non-hormonal options such as non-steroidal anti-inflammatory drugs (NSAIDs) and antifibrinolytics can be used effectively to treat heavy menstrual bleeding that is mainly cyclic or predictable in timing. (I-A)
12. Combined oral contraceptive pills, depot medroxyprogesterone acetate, and levonorgestrel-releasing intrauterine systems (LNG-IUS) significantly reduce menstrual bleeding and should be used to treat women with abnormal uterine bleeding who desire effective contraception. (I-A)
13. Cyclic luteal-phase progestins do not effectively reduce blood loss and therefore should not be used as a specific treatment for heavy menstrual bleeding. (I-E)
14. Danazol and GnRH agonists will effectively reduce menstrual bleeding, and may be used for scenarios in which other medical or surgical treatments have failed or are contraindicated. (I-C)
15. Patients receiving a GnRH agonist for longer than 6 months should be prescribed add-back hormone therapy, if not already initiated with GnRH agonist commencement. (I-A)

Surgical Management

Hysteroscopy Versus Endometrial Ablation

Clinical Tips
Key points for counselling women planned for endometrial ablation: 1. Confirm childbearing is complete 2. Require form of contraception 3. Rule out underlying uterine pathology (i.e., hyperplasia or malignancy) 4. Clearly outline expectations (patient satisfaction, not amenorrhea) 5. Discuss the risk of requiring a hysterectomy in the future

Summary Statement

- Non-hysteroscopic ablation techniques offer similar patient satisfaction results with fewer risks of complication and less anaesthetic requirement than traditional hysteroscopic ablation. (I-A)

Recommendations

16. The progestin intrauterine system has outcomes similar to endometrial ablation for women with heavy menstrual bleeding and thus may be considered prior to surgical intervention. (I-A)
17. In appropriate candidates, non-hysteroscopic ablation techniques should be the ablation methods of choice in view of their higher efficacy and safety than hysteroscopic techniques. (I-A)

Clinical Tip
Several non-hysteroscopic ablation techniques are currently available. Balloon, microwave, and radiofrequency ablation devices have a large reported clinical experience. One of the main advantages of these techniques is their successful implementation in a surgical suite or clinic setting, which avoids the use of operating room resources and general anaesthetic.

Hysterectomy

Summary Statement

- Hysterectomy provides definitive treatment for AUB. (I)

Fibroids

Clinical Tip
Fibroid localization with imaging is essential for appropriate management. SIS and hysteroscopy provide information on the location of intrauterine or submucosal fibroids. These types of fibroids are related to heavy menstrual bleeding. AUB not responding to medical treatment may be due to intracavitary lesions such as submucosal fibroids.

Summary Statement

- AUB secondary to submucosal fibroids may be managed by hysteroscopic myomectomy. (I)

Special Scenarios

Inherited Bleeding Disorders

Summary Statement

- Inherited bleeding disorders may be an underlying cause of AUB, with von Willebrand's disease present in the majority of cases. (II-2)

Recommendations

18. With the exception of NSAIDs, the same medical agents used to treat heavy menstrual bleeding among women with normal coagulation can effectively be used in the setting of inherited bleeding disorders. (II-1B)
19. Women with inherited bleeding disorders who have significant heavy menstrual bleeding or those who fail conventional medical therapy are best managed with a multidisciplinary approach. (III-C)
20. Hysterectomy planning or blood product therapy should be performed in consultation with a hematologist in patients with inherited bleeding disorders. (III-C)

Acute Bleeding

Summary Statement

- Acute heavy menstrual bleeding may result in significant anemia and emergent care. (III)

Recommendations

21. Acute heavy menstrual bleeding should be managed promptly and systematically to minimize patient morbidity and the need for blood transfusion. (III-C)
22. High-dose estrogen and tranexamic acid may help decrease or arrest acute heavy menstrual bleeding. (III-C)

The Adolescent

Summary Statement

- AUB in the adolescent most commonly represents ovulatory dysfunction related to immaturity of the hypothalamic-pituitary-ovarian axis. (II-2)

Clinical Tips
1. Selection of a medical therapy for AUB in adolescents should consider the need for contraception. Long acting reversible contraception may be considered first line therapy for both sexually active adolescents and, with individualized counselling, non-sexually active adolescents. 2. Oligomenorrhea at age 15 is highly predictive of persistent oligomenorrhea in early adulthood and warrants investigation.

Recommendation

23. For the adolescent presenting with heavy menstrual bleeding at or in close approximation to menarche, history and investigations should include an assessment for an underlying bleeding disorder. (II-2A)

Definitions:

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly randomized controlled trial

II-1: Evidence from well-designed controlled trials without randomization

II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group

II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

* Adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

Classification of Recommendations†

A. There is good evidence to recommend the clinical preventive action

B. There is fair evidence to recommend the clinical preventive action

C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making

D. There is fair evidence to recommend against the clinical preventive action

E. There is good evidence to recommend against the clinical preventive action

L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

† Adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.

Clinical Algorithm(s)

An algorithm titled "Management of AUB due to Fibroids" is provided in the original guideline document.

Scope

Disease/Condition(s)

Abnormal uterine bleeding

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Family Practice

Obstetrics and Gynecology

Surgery

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To provide current evidence-based guidelines for the diagnosis and management of abnormal uterine bleeding (AUB) among women of reproductive age

Target Population

Women of reproductive age

Interventions and Practices Considered

Evaluation

1. Thorough history and physical examination
2. Complete blood count
3. Sensitive urine or serum pregnancy test
4. Thyroid function tests
5. Testing for coagulation disorders
6. Transvaginal ultrasound
7. Saline infusion sonohysterography (SIS)
8. Hysteroscopy evaluation
9. Endometrial assessment and biopsy
10. Blood product therapy

11. Assess for an underlying bleeding disorder

Treatment

1. Non-steroidal anti-inflammatory drugs (NSAIDs)
2. Antifibrinolytics
3. Combined hormonal contraceptives (CHC)
4. Danazol
5. Gonadotropin releasing hormone (GnRH) agonists
6. Cyclic oral progesterone
7. Injected progesterone
8. Levonorgestrel-releasing intrauterine system (LNG-IUS)

Surgical Management

1. Endometrial ablation
2. Hysterectomy
3. Hysteroscopic myomectomy
4. Progestin intrauterine system

Major Outcomes Considered

- Quality of life
- Results of interventions including medical and surgical management
- Morbidity

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Published literature was retrieved through searches of MEDLINE and the Cochrane Library in March 2011 using appropriate controlled vocabulary (e.g., uterine hemorrhage, menorrhagia) and key words (e.g., menorrhagia, heavy menstrual bleeding, abnormal uterine bleeding). Results were restricted to systematic reviews, randomized control trials/controlled clinical trials, and observational studies written in English and published from January 1999 to March 2011. Searches were updated on a regular basis and incorporated in the guideline to February 2013.

Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly randomized controlled trial

II-1: Evidence from well-designed controlled trials without randomization

II-2: Evidence from well-designed cohort (prospective or retrospective) or case–control studies, preferably from more than one centre or research group

II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

*Adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

The committee reviewed relevant evidence in the English medical literature including published guidelines.

The quality of evidence in this document was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (see the "Rating Scheme for the Strength of the Evidence" and the "Rating Scheme for the Strength of the Recommendations" fields).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Classification of Recommendations†

A. There is good evidence to recommend the clinical preventive action

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L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

† Adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

The final document was reviewed and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada (SOGC).

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

General

- Appropriate diagnosis and medical and surgical management of abnormal uterine bleeding (AUB) in pre-menopausal women.
- Implementation of the guideline recommendations will improve the health and well-being of women with AUB, their families, and society.

Combined Hormonal Contraceptives (CHC)

- Menstrual regularity
- 20% to 50% reduction in menstrual blood loss (MBL)
- Reduction in dysmenorrhea and premenstrual syndrome (PMS)

Levonorgestrel-Releasing Intrauterine System (LNG-IUS)

- 70% to 97% reduction in MBL
- Amenorrhea in up to 80% at 1 year
- Reduced dysmenorrhea

Cyclic Oral Progesterone

Bleeding reduced by up to 87% with long phase regimen

Injected Progesterone

60% amenorrhea at 12 months, 68% at 24 months

Danazol

- 80% reduction MBL
- 20% amenorrhea
- 70% oligomenorrhea

Gonadotropin Releasing Hormone (GnRH) Agonists

Bleeding stopped in 89% by 3 to 4 weeks

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

- 20% to 50% reduction MBL
- Reduction in dysmenorrhea in 70%

Antifibrinolytics

40% to 59% reduction in MBL

Potential Harms

Combined Hormonal Contraceptives (CHC)

- Breast tenderness
- Mood change
- Fluid retention
- Breakthrough bleeding (BTB)
- *Rare*:
    - Venous thromboembolism (VTE)
    - Stroke
    - Myocardial infarction (MI)

Levonorgestrel-Releasing Intrauterine System (LNG-IUS)

- Irregular bleeding first 6 months
- Breast tenderness
- Acne
- Cramping
- Headaches

Cyclic Oral Progesterone

- Breast tenderness
- Mood changes
- Bloating
- Acne
- Headaches
- Weight gain

Injected Progesterone

- Irregular bleeding
- Breast tenderness
- Weight gain
- Mood changes
- Decreased bone mineral density (BMD) (reversible)

Danazol

- Weight gain
- Acne
- Muscle cramps
- Gastrointestinal (GI) upset
- Irritability

Gonadotropin Releasing Hormone (GnRH) Agonists

- Hypoestrogenic symptoms (hot flashes, night sweats, vaginal dryness)
- Bone pain
- Loss of BMD
- Mood changes
- Patients should be warned of the possible temporary "flare" or exacerbation of symptoms immediately after GnRH injection

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

- Indigestion
- Worsening/exacerbation of asthma
- Gastritis
- Peptic ulcers

Antifibrinolytics

- Indigestion
- Diarrhea
- Headaches
- Leg cramps

Contraindications

Contraindications

Combined Hormonal Contraceptives (CHC)

- History of venous thromboembolism (VTE) or stroke
- Uncontrolled hypertension (HTN)
- Smoking >15/day
- Over 35 years of age
- Migraine with aura
- Breast cancer
- Coronary artery disease (CAD)
- Active renal/liver disease

Levonorgestrel-Releasing Intrauterine System (LNG-IUS)

- Large intracavitary pathology
- Breast cancer
- Recurrent/recent pelvic inflammatory disease (PID)

Cyclic Oral Progesterone

- Pregnancy
- Breast cancer
- Liver disease

Injected Progesterone

- Pregnancy
- Breast cancer
- Active liver disease
- Liver tumours

Danazol

Liver disease

Gonadotropin Releasing Hormone (GnRH) Agonists

- Allergy
- Suspected pregnancy

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

- Allergy
- Renal disease
- Untreated HTN
- Platelet or coagulation disorders
- Active gastritis or peptic ulcers

Antifibrinolytics

Past history of VTE

Qualifying Statements

Qualifying Statements

This document reflects emerging clinical and scientific advances on the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Local institutions can dictate amendments to these opinions. They should be well documented if modified at the local level. None of these contents may be reproduced in any form without prior written permission of the Society of Obstetricians and Gynaecologists of Canada (SOGC).

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

Foreign Language Translations

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Singh S, Best C, Dunn S, Leyland N, Wolfman WL, Clinical Practice Gynaecology Committee. Abnormal uterine bleeding in pre-menopausal women. J Obstet Gynaecol Can. 2013 May;35(5 eSuppl):S1-28. [156 references]

Adaptation

Not applicable. The guideline was not adapted from another source.

Date Released

2013 May

Guideline Developer(s)

Society of Obstetricians and Gynaecologists of Canada - Medical Specialty Society

Source(s) of Funding

Society of Obstetricians and Gynaecologists of Canada

Guideline Committee

Clinical Practice – Gynaecology Committee

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Financial Disclosures/Conflicts of Interest

Disclosure statements have been received from all members of the committee.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the Society of Obstetricians and Gynaecologists of Canada (SOGC) Web site . Also available in French from the SOGC Web site .

Print copies: Available from the Society of Obstetricians and Gynaecologists of Canada, La société des obstétriciens et gynécologues du Canada (SOGC) 780 promenade Echo Drive Ottawa, ON K1S 5R7 (Canada); Phone: 1-800-561-2416.

Availability of Companion Documents

The appendix of the original guideline document contains a summary table of medical treatments for abnormal uterine bleeding.

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on September 27, 2013. The information was verified by the guideline developer on October 30, 2013. This summary was updated by ECRI Institute on September 18, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs).

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